A STUDY OF CLINICAL SPECTRUM OF 30 CASES OF HERPESZOSTER AND THERAPEUTIC TRIAL OF ACYCLOVIR VS FAMCYCLOVIR OF 10 CASES EACH

Dissertation Submitted in
fulfillment of the university regulations for

MD DEGREE IN
DERMATOLOGY, VENEREOLOGY AND LEPROSY

BRANCH – XX

CHENGALPATTU MEDICAL COLLEGE,
CHENGALPATTU.

THE TAMIL NADU
DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI.

MARCH 2010

CERTIFICATE

Certified that this dissertation entitled **"A STUDY OF CLINICAL SPECTRUM OF 30 CASES OF HERPESZOSTER AND THERAPEUTIC TRIAL OF ACYCLOVIR VS FAMCYCLOVIR OF 10 CASES EACH"** is a bonafide work done by **Dr. R.INDRADEVI**, Post graduate student of the Department of Dermatology, Venereology and Leprosy, Chengalpattu Medical College, chengalpattu, during the academic year 2007 – 2010. This work has not previously formed the basis for the award of any degree.

Prof. Dr. P.C .CHITTAMBALAM, MD.DD
Professor and Head of the Department,
Department of Dermatology and Leprosy,
Chengalpattu Medical College,
Chengalpattu

Prof. Dr.P.PARASAKTHI, MD,
DEAN INCHARGE,
Chengalpattu Medical College,
Chengalpattu.

ACKNOWLEDGEMENT

I would like to express my sincere and heartfelt gratitude to **Prof.Dr.K.MANOHARAN.MD.DD,** Professor and Head, Department of Dermatology. I am greatly obliged for his unvarying attention and encouragement.

I am extremely thankful to **Prof. Dr. P.C CHITTAMBALAM, MD.DD,** Professor and Head**,** Department of Dermatology and **Prof.Dr.G.SRINIVASAN, MD.DV,** Professor and Head, Department of Venereology, Chengalpattu medical college, for their valuable guidance and whole hearted support.

I express my earnest gratitude to **Dr.T.K.ANANDHI, Dr.B.VIJAYALAKSHMI,** and **Dr.S.MURUGAN**, Assistant professors of Department of Dermatology and venereology, Chengalpattu medical college, for their kind advice and cooperation.

I am thankful to **Dr.R.SINDHUJA, Dr.D.VARALAKSHMI, and Dr. C.CHANDRAKALA,** Tutors of Department of Dermatology and venereology**,** Chengalpattu medical college, for their valuable support.

My sincere thanks to **Prof. Dr.R.JAGANNATHAN MD.DCH**, The Dean Incharge of Chegalpattu medical college Hospital, Chengalpattu, for allowing me to do this Dissertation and utilize the institutional facilities.

Due credit goes to my juniors, lab technician, and staff members for their support throughout my study.

I am profoundly grateful to all my patients for their whole hearted co operation and participation in this study.

CONTENTS

INTRODUCTION

Varicella Zoster virus (VZV) belongs to Herpesviridae family

(Sub family: Alpha herpesviridae).

Herpes viruses measure approximately 200 nm in diameter and contain linear, double stranded DNA core enclosed within a protein capsid, covered by a tegument and glycoprotein containing envelope. Biological properties unique to herpes viruses include latency and reactivation.

Varicella zoster (Chicken Pox) and Herpes zoster (Shingles) are caused by same varicella zoster virus.

Herpes zoster is a localized disease characterised by multiple superficial painful grouped vesicles on an erythematous base involving a particular dermatome due to reactivation of varicella zoster virus that is lying dormant in sensory ganglion.

Most often Varicella is a self-limited infection of childhood. Zoster is mainly a disease of adults. A prerequisite for developing zoster is a prior episode of varicella, which on occasion may have been sub-clinical.

During Varicella infection, Varicella zoster virus remains latent inside the sensory nerve ganglion. Zoster results when the latent virus reactivates and returns from the ganglion to infect the skin.

Most often Varicella zoster virus reactivation occurs in the setting of relative immunological compromise, such as aging, local trauma immunosuppression (Steroids, HIV), frontal sinusitis, radiation and tumor involvement of spinal cord.

REVIEW OF LITERATURE

History

The term ‘HERPES’ has been used in medicine since from Hippocrates and is derived from Greek word “Erpein” meaning “to creep” The term “Zoster” also a Greek word meaning “Girdle” ascribes the rash has belt like appearance. The other commonly used synonym “Shingles” is derived from the Latin word cingulum or singlullus. One more synonym for zoster is “Zona”. The Norwegians call zoster as “belt of roses from hell” and Danes calls it “hell fire” a very apt.

The relationship of zoster to varicella was first noted by Hungarian pediatrician VonBokay (1888). After that Kondrafitz (1925) and Brunsgaard confirmed that same agent was responsible for both varicella and zoster (1932) Seiler (1949) and Hope Simpson (1954) also reported epidemiologic evidence that zoster and varicella were caused by same virus. Later Lipschutz 1921 reported that zoster lesions were identical histologically to that of varicella as previously described by Tyzzer. Zoster occurs due to reactivation of latent virus .This was first suggested by Garland (1943) and later Hope-Simpson (1965) reasoned that it is due to reactivation of latent virus occurring since the primary infection.

Epidemiology

Incidence 3.4 cases per 1000(Hope –Simpson and Ragozzino etal 1945-1959), No racial or seasonal prediction. Both sexes equally affected. Incidence increases with age. 2/3 cases occur in individuals over 50 years of age. Less than 10% of cases occur below the age of 20 years, Life time incidence of HZ was observed to be 10-20% in general population and an annual incidence of 600,000 to 850,000 cases of HZ have been reported in U.S. Spread –Direct contact, Aerosol.

Virology of zoster

HZ is caused by varicella –Zoster virus (VZV), same virus causing Varicella. Previously called as herpes virus varicella.It is a DNA virus belonging to subfamily of herpes viridae family and also designated as Human herpes virus 3.

Structure

Electron microscopically varicella zoster virus is a typical herpes like particle, 150-200 nm in diameter, with a lipid envelope bearing glycoprotein spikes (peplomers). The central region of virus contains an icosahedral nucleocapsid composed of 162 capsomere within which is the viral genome.

Between the nucleocapsid and the envelope is an amorphous, protein filled space known as tegument .Five families of viral glycoprotein have been identified, gpI,gpII,gpIII,gpIV,gpV and they are the primary markers for both humoral and cell mediated immunity.

Pathogenesis

Herpes zoster is the result of reactivation of endogenous virus that had persisted in latent form within sensory ganglia following an earlier attack of varicella.

Latency

Varicella zoster viral DNA is localized primarily in trigeminal and thoracic ganglion , corresponding to dermatomes in which chicken pox lesions are maximal and which are most commonly involved by zoster presumably because areas of skin with a dense rash during.varicella transmits larger amounts of virus to corresponding sensory ganglia and thus establishing latency in large number of ganglionic cells. Subsequently reactivation occurs at random and it is in these maximally infected ganglia with their corresponding innervated skin manifest the lesions more frequently. Two concepts prevail about the establishment of infection in ganglia.

One during the course of varicella, vzv passes from lesions in skin and mucus membranes into contiguous sensory nerve endings, and then to sensory ganglia or alternatively, varicella zoster virus might also reach the ganglia via the blood stream during the course of primary or secondary viremia of varicella.

Reactivation

The level of antibody is considered to be the critical determinant of host's capacity to contain VZV reversion. Based on number of studies conducted at various places, it now appears that cellular immunity (CMI) is more important, principally that of T lymphocytes in host resistance to this recurrent VZV infection of endogenous origin.

The mechanisms involved in the activation are unknown .Most patients are otherwise healthy without any predisposing factors. Conditions associated with increased occurrence include immunosuppression in HIV infection and Hodgkin's disease and other malignancies like lymphocyte and granulocytic leukemia or other malignancies, administrations of immunosuppressive drugs and corticoids, irradiation of spinal column tumor involvement of cord, dorsal root and adjacent structures, local trauma, surgical manipulations of spine, heavy metal poisoning and therapy (arsenic) and frontal sinusitis for precipitant of ophthalmic zoster in 16% cases. Virus multiplies and spread with in the ganglion, causing neuronal necrosis and

intense inflammation. The VZV spreads antidromically down the sensory nerve with in the axon sheath and is released around sensory nerve endings in skin, where multiplication of virus within the epidermal cells causes swelling, and vesicle formation due to edema, spread of ganglionic infection proximally along the posterior nerve root to meninges and cord results in local leptomeningitis, cerebrospinal fluid pleocytosis and segmental myelitis.

Infection of motor neurons in anterior horn and inflammation of anterior nerve root account for local palsies that may accompany the cutaneous eruption and extension of infection within the central nervous system may result in rare complications of herpes zoster such as meningoencephalitis and transverse myelitis.

Pathology

Cutaneous lesions

Early stage

An early papular lesion, the epithelium is slightly elevated due to swelling of infected epithelial cells and to edema and vascular congestion of underlying dermis. In the superficial dermis, capillary endothelial cells are swollen, and they often contain typical intranuclear inclusion bodies. Similar inclusion bodies may be seen in nuclei of fibroblast in the surrounding connective tissue, which is edematous and infiltrated by small number of

mononuclear cells. Superficial lymphatics are dilated and cells lining these structures are also swollen and may contain intranuclear inclusion bodies, cells of germinal layer and the deeper portion of stratum spinosum are involved initially and show ballooning degeneration due to viral multiplication with loss of intracellular bridges and are soon separated by intercellular edema (Secondary acantholysis).Only few small multinucleated giant cells possessing 3-8 nucleus are seen at this stage. The epithelium is only slightly elevated.

Vesicular stage

As a result of infection and degeneration of increasing number of cells, fusion of adjacent areas of degeneration and continuing influx of edema fluid (reticular degeneration), the papule transform into a vesicle, the roof being formed by upper malphigian and horny layers. The cellular vesicle fluid contains fibrin, ballooned epithelial cells, and abundant cell free viral particles, Multinucleated giant cells contain upto 15 nuclei which are nothing but fused epithelial cells containing eosinophilic intranuclear inclusion bodies (Lipschutzbodies formely cowdry typeA bodies) of 3-8 nm diameter. The upper dermis beneath the vesicle contain inflammatory infiltrate, mainly of lymphocytes, monocytes and some eosinophils and neutrophils.

Late Stage

Invasion of polymorphonuclear leucocytes and a small number of macrophages from underlying dermis, invade the vesicles transforming them into pustules. The fluid is then absorbed, with the formation of a flat adherent crust that is eventually detached by regrowth of subjacent epithelial cells. The evolution from papule to early crusting normally occurs over a period of 24- 48 hrs. Lesions of uncomplicated varicella heal with out scarring.

Mucous membrane lesion

Lesion in mucous membranes develop in the same way as cutaneous lesion but the roof of the vesicle rupture quickly to produce a shallow ulcer that heals rapidly.

Clinical features

Prodrome of Herpes zoster

Initial Symptoms are usually pain and paresthesia in the involved dermatome, preceding the eruption by 1-4 days ,and varies from superficial itching ,tingling or burning to severe, deep boring or lancinating pain .It may be constant or intermittent and is accompanied by tenderness and hyperesthesia of involved dermatome which is a useful predictive sign for diagnosis .The pre-eruptive pain may stimulate migraine headache, pleurisy,

myocardial infarction, duodenal ulcer,cholecystitis, biliary or renal colic, appendicitis, prolapsed intervertebral disc or early glaucoma depending upon the level of involvement which may lead to serious misdiagnosis.

Constitutional symptoms including headache, fever occur in about 5% pts, usually in children and may proceeded the rash by 1-2 days and gradually subside as the eruption appears. A tender, regional lymphadenopathy is present in most of cases at this stage.

Some patients experience acute segmental neuralgia without being followed by a cutaneous eruption called as “Zoster sine eruptione”.Zoster sine eruption, presumably reflecting an aborted eruption, and the concurrent rise in antibodies to VZV provides evidence that it is due to herpes zoster. A few other patients may never experience skin lesions but have pain or visual or ocular lesions which may be severe. Although facial palsy frequently complicates (Ramsay-Hunt syndrome) VZV infection does not appear to be responsible for most cases of idiopathic facial palsy (Bell’s palsy)

Eruptive phase

The most distinctive feature of Zoster is localization of rash, which is nearly always unilateral does not cross the midline and is generally limited to the area of skin innervated by a single sensory ganglion, though one or 2 adjacent dermatomes may be involved. Occasionally, a few vesicles appear

to cross the midline on the opposite side, owing to transverse nerve twigs. Eruption is rare in bilaterally symmetric or asymmetric dermatomes .Herpes Zoster tend to in volute more slowly and usually consist of closely grouped vesicle on an erythematous base, rather than the more discrete, randomly distributed vesicles of varicella .The lesion begin as erythematous macules and papules which often first appear where superficial branches of the affected sensory nerve are given off.

E.g. Posterior primary division and the lateral and anterior branches of anterior primary division of spinal nerve .Vesicles form within 12-24 hrs in clusters from the erythematous and the edematous base (i.e, inflammatory base) and evolve into pustules by day 3 or 4 successive crops continue to appear for up to 7 days, usually 1-4 days. Vesicles either umblicate or rupture before forming a crust in 7-10 days which generally fall off in 2 to 3 weeks in normal individuals. Patient is considered to be contagious for about 7 days after the appearance of rash till the crusting stage. The rash is most severe and lasts longer in older people and is least severe and of shorter duration in children. Pain generally remits as the crusts fall off but may persist for longer even after the healing of rash and may intensify later. Segmental pain, prominent feature of Zoster in older person and it is seldom a significant symptom in children.

Herpes Zoster occurs with greatest frequency in those areas in which the rash of varicella was most abundant. The trunk from T3 to L2 division and ophthalmic division of trigeminal nerve most frequently affected and rarly lesions occur below the knee and elbow. But in infants and children, localization to cervical with lumbosacral region is characteristic.

In order of frequency it has been reported, in adult to affect thoracic dermatome in 50-55%, cranial nerves 15-20%, cervical dermatome 14%, lumbar 14% and sacral 2%

The elderly or debilitated patients may have prolonged and difficult course. For them, the eruption is typically more extensive and inflammatory. Occasionally resulting in hemorrhagic blisters, skin necrosis, secondary bacterial infection or extensive scarring, which is sometimes hypertrophic or keloidal.

Clinical types of herpes zoster

Thoracic zoster

Cervical zoster

Trigeminal zoster

Lumbosacreal zoster

Clinical zoster variations

Disseminated herpes zoster

Herpes zoster with aberrant vesicles

Herpes zoster at two different sites

Zoster sine herpete

Bilateral zoster

Recurrent zoster

Zoster Ophthalmicus

Zoster oticus or Ramsay hunt syndrome

Glosssopharyngeal & Vagal zoster

Sacral Zoster

Zoster encephalomyelitis

Zoster Hemiplegia syndrome

Dermatological dyspnoea –Diaphragm

Phantom hernia

1. Trigeminal nerve zoster

The fifth cranial nerve or trigeminal nerve has 3 main divisions, namely ophthalmic, maxillary and mandibular. The ophthalmic division further divides into three main branches ,namely frontal,lacrimal and nasociliary

nerves. Frontal nerves in turn divides into supraorbital and supratrochlearnerves. Involvement of any branch of ophthalmic nerve is called “Herpes zoster ophthalmicus”

a. Herpes zoster ophthalmicus

10-15 % cases of Herpes Zoster involve the ophthalmic division of trigeminal nerve. The rash of ophthalmic zoster may extend from level of eye to the vertex of skull, but it does not cross the midline of forehead. Nasociliary branch supplies the tip and sides of nose and intra ocular structures. Nasociliary involvement which occurs in 30-40% of ophthalmic nerve involvement, vesicle on tip and side of nose (Hutchison’s sign) is associated with most serious ocular complication including conjunctivitis commonly and rarly keratitis, scleritis, uveitis extra ocular palsies very rarely.

Frontal sinusitis preceded 16% of all cases of ophthalmic Herpes Zoster. Patients with ophthalmic herpes zoster who are HIV negative tend to have less severe infection and also recover faster than those, who are HIV positive. Herpes Zoster ophthalmicus is a known marker of HIV/AIDS in Africa.

b. Herpes zoster of Maxillary division of trigeminal nerve.

Zoster of maxillary divisions of trigeminal nerve produces vesicles on palate, uvula and tonsillar area.

c. Herpes Zoster of mandibular division of trigeminal nerve.

Zoster of mandibular divisions of trigeminal nerve produces vesicles on anterior part of tongue, floor of mouth and buccal mucosa.In oro-facial zoster, tooth aches may be the presenting symptoms since alveolar braches of this division supply the periodontal structures.

2. Facial nerve

Involvement of geniculate ganglion leads to a triad of facial palsy in combination with herpes zoster of external ear or tympanic membrane (Herpes zoster oticus) with or without tinnitus, vertigo and deafness (in 37% patients) the so called “Ramsay Hunt syndrome” This results from compression of facial and auditory nerves probably caused by swelling of sensory fibres, while passing through the confined spaces of facial canal of internal auditory meatus. Involvement of special sensory fibres may lead to painful vesicles on uvula, palate and anterior part of tongue, associated with loss of taste sensation over the anterior two third of ipsilateral side of tongue. Sensory fibres from facial nerve innervate deep facial tissues, hence jaw pain stimulating a dental abscess is often present.

3. Glossopharyngeal (ix) and vagal(x) nerve

Glossopharyngeal Zoster produces pain in ear and pharynx and vesicles and ulcer on soft palate and ear. Vagal zoster may produce vesicles on base of tongue, epiglottis and arytenoids and may cause paresis of larynx and pharynx as well as cardiac and epigastric distress.

Cervical zoster

Zoster of upper cervical roots (C2,C3,C4) produce lesions on the scalp, neck retro auricular region known as “Herpes occipitocollaris” and this may be associated with “Ramsay Hunt syndrome” (can also involvement of IX,X cranial nerves). With lesions of cervical nerve II (also cranial nerve V) in scalp, alopecia may rarely occur and may lead to scarring lower cervical roots involvement affects the upper limbs.

Thoracic zoster

Thoracic dermatomes are most frequently affected (55%) than the other dermatomes .The rashes are nearly always unilateral localized and do not cross the midline, and is generally limited to the area of skin innervated by a single sensory ganglion. Pain in the thoracic dermatome leads to a misdiagnosis of peptic ulcer disease, gall bladder diseases, renal colic and myocardial infarction. Abdominal hernia occurs especially in zoster involving the thoracic dermatome T10 - T11.Electrocardiographic changes

sometimes may be noted with left upper thoracic zoster and galactorrhea in females has been reported with zoster involving the mammary areas.

Sacral zoster (s2,s3.s4)

Cutaneous lesions are limited to a narrow segment on posterior aspect of calf and thigh for S2 dermatome and perianal region of gluteal skin for other roots. Sacral zoster is mainly associated with bladder and/or bowel dysfunction due to migration of virus to adjacent autonomic nerves, leading to urinary hesitancy or urinary retention.

Bilateral herpes zoster

Herpes Zoster is almost always unilateral. The rarity of bilateral cases is indicated by individual case reports in the literature.

Herpes zoster with multiple unilateral lesions

This type is quite rare and most likely to be noted in persons with some severe systemic illness i.e. Hodgkin's lymphoma, metastatic cancer, HIV etc. such disease should be looked for when this dermal distribution is encountered.

Recurrent herpes zoster

Recurrent attacks are rare and zoseriform herpes simplex should always be noted out.

Zoster in malignancy

Herpes zoster has been reported with Hodgkin'slymphomas, leukemias, metastatic cancer and other neoplasm. The presence of Herpes Zoster especially in an older person indicates the need for searching for these diseases as a causative background. Use of cytotoxic immunosuppressant therapy altering immune response may also be a factor.

Herpes zoster in HIV infection

Herpes zoster is included in clinical stage -II of WHO staging system for HIV infection.

Herpes Zoster occurring in HIV disease is usually typical in involving one or two adjacent dermatomes but uncommonly it may be multidermatomal, recurrent within the same dermatome or disseminated. The eruption may be bullous, hemorrhagic, necrotic and may be accompanied by severe pain.

The majority of HIV infected patients with herpes zoster experience an uneventful recovery, however atypical clinical course of herpes zoster is not uncommon. Lesions may persist for months, either in localized or disseminated form, appearing as hyperkeratotic, ulcerating, painful nodules, often with central crusting or ulceration with a border of vesicles.

Systemic dissemination of herpes zoster with hepatitis, encephalitis and pneumonitis is common. HIV infected patients with herpes zoster show increased neurological and ophthalmic complications particularly retinal necrosis. Reactivation of varicella zoster virus is the commonest cutaneous manifestation of immune restoration disease.

Herpes zoster in children

Herpes zoster in neonates and children may represent the result of an attenuated response to intrauterine or neonatal infection. Baba et al reported that children who had varicella before 2 months of age has lower Varicella zoster antibody titres and diminished skin test reactions, thus reactivation in these cases may be secondary to an abnormal immune response to primary infection by Varicella.

The development of herpes zoster is often preceded by radicular pain and is less common in children. Malaise, headache and fever may precede the rash, particularly in younger patients. Resolution of lesion occurs within 1-3 week.

Both normal and immunosuppressed patients may have generalization of herpes zoster. Post herpetic neuralgia is uncommon in children. Immunocompromised children with herpes zoster may have more extensive involvement with a higher risk of viremia and visceral dissemination.

Herpes zoster in pregnancy

Herpes Zoster during pregnancy whether it occurs early or late in pregnancy appears to have no deleterious effects on either the mother or infant. Maternal zoster in pregnancy is not associated with intrauterine infection .But maternal varicella in the first 20 weeks of pregnancy is associated with a approximate 2% risk of fetal damage.

Complications

A. Acute complications of herpes Zoster

Acute complications occur during the course of illness and are more common in immunocompromised individuals.

i. Cutaneous complications

The common cutaneous complications are secondary bacterial infections, cutaneous necrosis, scarring, and dissemination and gangrene formation.

ii. Ocular complications

Ocular complications include uveitis, keratitis, conjunctivitis, conjuctival edema, ocular muscle palsies, proptosis, sclerosis, retinal vascular occlusion and ulceration scarring and even necrosis of lid. Involvement of ciliary ganglion may give rise to Argyl-Robertson pupil.

Acute retinal necrosis caused by varicella zoster virus occasionally occurs in immuno competent patients, although more recent studies have focused on ocular disease in HIV infected patient.

iii. Neurological complications

This includes cranial neuritis, motor neuropathy, autonomic neuropathy, aseptic meningitis, meningo-encephalitis, transverse myelitis, necrotizingmyelopathy, Guillain-barresyndrome, hemiplegia and granulomatous angitis.

a. cranial neuritis

Cranial neuritis includes Trigeminal nerve zoster (Herpes zoster ophthalmicus, maxillary and mandibular, nerve zoster), Ramsay-Hunt syndrome with involvement of facial nerve and 8th cranial nerve, Vagus and Glosso pharyngeal nerve zoster.

b. Motor neuropathy

This occurs in 5% cases and is more common in older patients and those with malignancy and in cranial when compared with spinal nerve involvement .The motor weakness usually follows the pain and the eruption by a few days to a few weeks ,but occasionally precedes or accompanies them. The affected segment is usually but not always the same. Complete recovery is expected in 55 % and significant

improvement in a further 30% of cases .In ophthalmic zoster ocular palsies occur in 13% and facial palsies in 7%.An abdominal hernia followed zoster involving thoracic 10th and 11th motor roots. Zoster of anogenitial area may be associated with disturbances of defecation or urination Herpes zoster oticus accounts for about 10% of cases facial palsy .Glossopharyngeal and vagal zoster produces pharyngeal with palatal muscle weakness. Zoster of 2nd to 4th cervical nerve may paralyse the ipsilateral diaphragm due to involvement of phrenic nerve.

c. Autonomic neuropathy

Autonomic nerves system may also be affected. Autonomic nerve involvement often present as bladder dysfunction .Gastrointestinal involvement present as spasm hypotonia or ileus.

d. Herpes Zoster Meningo encephalitis

Neurological symptoms characteristically appear within the first 2 weeks of onset of skin lesions. Patients at risk are those with trigeminal and disseminated zoster as well as the immunosuppressed. Rarely manifestations of a meningoencephalitis may be significant and at times severe enough to cause death.

e.Granulomatous angitis (or) Delayed contralateral hemiparesis

By direct extension along the intracranial branches of trigeminal nerve, VZV gains access to the CNS infects the cerebral arteries. Patients presents with headache and hemiplegia.

f. Herpes Zoster myelitis

More rarely, the myelitis lesion predominates in zoster or is the sole feature, so that the clinical picture is one of acute onset of paraplegia from a diffuse involvement of spinal cord. The picture is that associated with acute, transverse myelopathy.

IV. Visceral complications

Patients with lympho-prolifearative malignancies are at risk for cutaneous dissemination and visceral involvement including varicella pneumontits, hepatitis and meningo encephalitis.

B. Complications occurring after resolution of herpes zoster lesion

The commonest and most intractable sequel of zoster is post herpetic neuralgia, generally defined as persistence or recurrence of pain for more than a month after the onset of zoster, but better considered after 3 months. It occurs in about 30% of patients over 40 years of age and is most frequent when trigeminal nerve is involved.

The pain has two main forms. A continuous burning pain with hyperesthesia and spasmodic shooting type, although a pruritic ‘crawling paraesthesia may occur. Allodynia, pain caused by normally innocuous stimuli, is often the most distressing symptom and occurs in 90% of people with post herpetic neuralgia

Patho-physiology of pain

A Number of different overlapping mechanisms appear to be involved in the pathogenesis of pain in herpes zoster and post herpetic neuralgia.

Injury to the peripheral nerves and to neurons in the ganglion triggers afferent pain signals. Inflammation in the skin triggers nociceptive signals that further amplify cutaneous pain. The abundant release of excitatory amino acids and neuropeptides induced by the sustained barrage of afferent impulses during the prodrome and acute phase of herpes zoster may caused excito-toxic injury and loss of inhibitory interneurones in spinal dorsal horn

2. Post –Herpetic itch

Many patients with shingles experience neuropathic itch accompanying pain or itch may be present instead of pain.

3. Progressive multifocal leuko-encephalopathy

In addition to latent infection VZV can produce prolonged smoldering sub clinical infection in patients lacking normal defenses to eliminate the viral infected cells and resulting in cell-cell spread of infection.

4. Scarring

Elderly malnourished, debilitated or immunosuppressed patients tent to have a more virulent and extensive course of disease and scarring. Types of scarring seen in zoster are

- Atrophic
- Hypertrophic
- Keloidal
- Vitiligenous
- Pitted pigmented (anaesthesia dolorosa)

5. Inflammatory skin lesions following a zoster infection (Isotopic response)

Following zoster, inflammatory skin lesion may rarely occur with in the affected dermatome. Lesions usually appear with in a month and rarely, longer than 3 month after zoster.

Lesions reported in herpes zoster scar include a keloid, comedones, lichenplanus, giantcelllichenoid dermatitis, urticaria, anulomatous vasculitis, granulomatous folliculitis, sarcoidosis, LSA, Morphea,

eosinophilic dermatosis, fungal infections, Pseudo lymphoma, lymphoma, leukemia cutis, Rosai Dorfman disease, Kaposi's sarcoma, various skin cancers and metastasis.

Diagnosis of herpeszoster

i. Clinical diagnosis

Most of the cases, zoster is diagnosed by its clinical features.

ii. Laboratory diagnosis

1. Morphological test

Tzanck smear

Initial test of choice is a cytological smear (Tzanck smear). Test does not differentiate herpes simplex from zoster. The base of an early lesion is scraped and stained with Hematoxylin eosin (H&E),Leishmans, Giemsa, wrights, toludineblue ,Paponicolou ,or paragonmultiple stain. The presence of multi nucleated giant epithelial cells and ballooning cells containing intranuclear acidophilic inclusion bodies distinguishes the cutaneous lesions produced by VZV from all other vesicular eruptions except those produced by herpes simplex virus. Overall it is positive in 80% of clinically suggestive lesions and positively high with vesicles and low with pustules and with crusts. Experience of the examiner is also important in interpretation.

2. Skin Biopsy

Biopsy facilitates reliable diagnosis even in the prevesicular stage and provides more material for histological examinations, and it is easier to interpret than Tzanck Smear and of greatest value when gross morphology is not diagnostic or characteristic, as in atypical lesions such as the chronic verrucous lesion produced by acyclovir resistant vzv in patients with AIDS. Biopsy can be done by shave, punch or wedge excision technique. Ballooning degeneration is peculiar to viral vesicles, ballooning degeneration is found mainly at the base of vesicle, reticular degeneration is seen on its superficial aspect and margin. The upper dermis shows inflammatory infiltrate composed of lymphocytes, monocytes and few eosinophils.

3. Virological Investigations

a. Viral culture

The most definitive test is a positive viral culture from vesicular fluid, but a minimum of 48-72 hrs required to produce the diagnostic cytopathic effects. Infective material is inoculated into human amnion, human fibroblast, HeLa or verocells .

B. Varicella zoster virus antigen detection

VZV antigen may be demonstrated by immunofluorescence, using a commercially available monoclonal antibody to VZV that is conjugated to fluorescein.

c. Electron Microscopy

The ultrastructral features of varicella zoster virus are similar to those of Herpes simplex virus. However colloidal gold immuno electron microscopy using monoclonal antibodies can distinguish between the two conditions.

4. Serological test

A number of sensitive serological tests are available to measures antibodies to VZV

Serological tests include

1. Fluorescent antibody to membrane antigen (FAMA)
2. Latex agglutination test.
3. Enzyme linked immunosorbent Assay (ELISA)
4. Enzyme Immuno Assay (EIA)
5. Immune adherence hemagglutination assay (IAHA)
6. Radio Immuno Assay (RIA)

7. Complement fixation test (CFT)

8. Varicella Zoster virus neutralization tests.

5. Newer Techniques

1. Nucleic acid probe

The Nucleic acid hybridization test has also been described for the detection of Varicella zoster virus DNA sequences in clinical specimens. The Spot hybridization assay used was comparable to cell culture in sensitivity and specificity.

2 .Polymerase Chain Reaction

PCR is more sensitive than viral culture or Tzanck smear for detecting VZV infections. PCR was described as particularly useful for rapid and specific diagnosis of VZV infection without the practical and technical limitations of conventional viral isolations or Tzanck smears.

Treatment

The aim of treatment is the suppression of inflammation, pain and infection.

General

Non Specific Topical Therapy

Topical cool compresses, calamine Lotions, Burrow's solution, Corn starch baking Soda, 1% gentian violet paint can be used. Occlusive ointments and steroid containing lotions and cream should be avoided. Topical antibiotic ointments can also be used in case of secondary infection (eg.1% Silver sulphadiazine, soframycin, mupirocin etc.)

Specific

1. Specific Topical therapy

Idoxuridine in dimethyl sulphoxide,5% acyclovir ointment,1% topical trifluoro- thymidine, topical preparation of acyclovir ointment or solution effective in keratouveitis in ophthalmic zoster, but topical therapy of antiviral agent are not effective in HZ rash.

2. Antibiotics

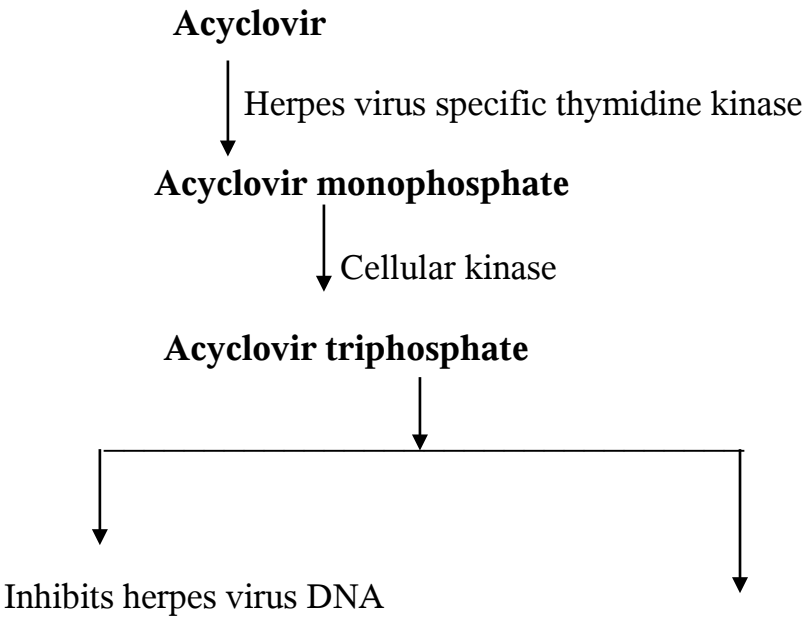
Are useful for secondary bacterial infections.

Antiviral therapy

1. ACYCLOVIR

Synthetic purine nucleoside, Deoxy guanosine analogue,
Specific against herpes viruses, Very active against HSV and VZV
Less active against CMV and EBV.

Mechanism of action



Oral acyclovir significantly reduced the healing time, duration of viral shedding and acute pain in randomized controlled trials in patients older than 50 years of age who were treated within 72 hours of rash onset.

Oral dose: 800 mg 5 times a day for 7 days.

Children: 20 mg /kg /Bwt , Maximum tolerated dose: 40mg/kg/Bwt

IV dose: 10 mg / kg Q8H for 7 days.

Indications

1. Immunocompetent persons with age 50 years or above
2. Ophthalmic Zoster
3. Localised zoster
4. Disseminated Zoster
5. Chronic severe zoster in AIDS patients.
6. Ramsay Hunt syndrome.
7. Visceral complications

2. FAMCYCLOVIR

Famciclovir is an ester prodrug of guanine nucleoside analogue penciclovir. It is converted in the intestine and liver to pencyclovir.

Penciclovir is phosphorylated to penciclovir triphosphate which in turn inhibits viral DNA polymerases and also inhibits extension of nascent viral DNA chain.

Dose: 500 mg TDS for 7 days

3.VALACYCLOVIR

It is the L-valine ester of acyclovir. It was developed to provide increased oral bioavailability of acyclovir. Valacyclovir may be more effective in resolution of zoster associated pain.

Dose: 1 gm TDS for 7 days.

4. FOSCARNET (TRI SODIUM PHOSPHONOFORMATE)

It is a pyrophosphate containing compound that is active in vitro against Varicella zoster virus.

Foscarnet noncompetitively inhibit viral DNA polymerases at the pyrophosphate binding sites

Dose: 40 mg /kg IV Q8Hrly for 14 -21 days.

Followed by a maintenance does of 120 mg /kg /day.

5. CIDOFOVIR

It is a phosphonate nucleotide analogue. It has activity against a broad range of herpes viruses. Cidofovir does not require initial phosphorilation by virus induced kinases, but is converted by host cell enzymes to cidofovir diphosphate which is a competitive inhibitor of viral DNA polymerases and to a lesser extent to host cell DNA polymerase,

6. VIDARABINE (ADENINE ARABINOSIDE)

It is an adenosine analogue which is phosphorylated intracellular by host enzyme and rapidly metabolished to hypoxanthine arabinoside by

adenosine deaminae, resulting in markedly reduced antiviral activity within the cells. This instability and systemic toxicity have limited its use.

Dose: 10 mg / day infused over 12 hrs for 5 days.

7. IDOXURUDINE

This synthetic nucleoside is effective against DNA viruses, particularly the herpes group. Its use is now restricted to topical application because of severe bone marrow and hepatic toxicity when given intravenously.

RECENT DRUGS

1. Sorivudine

It is an uracil analogue with activity against VZV infection. It requires viral thymidine kinase for phosphorylation.

2. Brivudine

It is a new uracil derivative with potent and specific activity against VZV. It is effective in a single or twice daily doss orally (50-200 mg) in immunocompetent adults and older patients. In immunocompromised patients. It is as effective as IV acyclovir in doss of 125 mg tab every 6 hours.

3. Oral enzyme therapy

Oral enzyme therapy is beneficial in disease characterized in part by TGFβ over production that included shingles patients.

4. Human Interferon-A

Interferons are synthesized by DNA recombinant technology. Its nonspecific antiviral effects, involving synthesis of RNA and additive protein with immunomodulatory effects help in preventing VZV synthesis and elimination of infected cells.

Role of steroids in herpes zoster management

Combination therapy of steroid and acyclovir resulted in an improved quality of life, as measured by reduction in use of analegesics, the time to uninterrupted sleep,and the time to resumption of usual activities. However, neither study demonstrated any effect of steroids on the incidence or duration of post herpetic neuralgia.

Treatment of acute pain associated with herpes zoster

For acute pain scheduled short acting narcotic analgesics should be prescribed. For persistent pain, long acting controlled release opioids are preferred. If pain control remains inadequate, then regional or local anesthetic nerve blocks should be considered. The effectiveness of

carefully managed opiates, and tricyclic antidepressants during the acute phase of herpes zoster in reducing the incidence, duration and severity of

PHN is not known. Intradermal steroids, xylocaine and epinephrine can also be given.

Treatment of post herpetic neuralgia

Topical therapy

Topical lidocaine patch

Topical EMLA cream

Topical capsaicin (0.025%) cream

Topical aspirin tablets in chloroform

Doxepin cream (5%)

Systemic treatment

1. Anticonvulsants

For stabbing pain sodium valproate, clonazepam, carbamazepine and gabapentin are effective.

2. Tricyclic antidepressants

Desipramine, nortriptyline, maprotiline amitriptyline are effective in post herpetic neuralgia. They are thought to act independent of their antidepressant action.

3. Oxycodone

Controlled release oxycodone (10mg every 12 hrs) is an effective analgesic for the management of steady pain, paroxysomal spontaneous pain and allodynia.

4 .Analgesics

Aspirin and other NSAIDS are commonly used in patients with post herpetic neuralgia but their value is limited. Tramadol a centrally acting analgesic with opioid and non opioid activities also effective in post herptic neuralgia(Maximum dose 600 mg / day)

5 .Antipsychotic

Fluphenazine, chloroprothixene and perphenazine are used with other drugs.

Other modalities of treatment

- Intrathecal methyl prednisolone
- Intradermal steroids, xylocaine and epinephrine injection.
- Sympathetic blocks (Stellate ganglion or epidural) with 0.25%

  Bupivacaine prevents or relieves post herpetic neuralgia.

  Epidural injection are made at or just above the highest

  dermatome of rash .

- TENS(Transcutaneous electrical nerve stimulation) may be helpful,
- Acupuncture
- Spinal cord stimulator
- Biofeed back
- Jaipur block

This consists of local subcutaneous infiltration of 2 % lignocaine, 0.5% bupivacaine and 4 mg per ml.dexamethasone,2.5ml each taken in a syringe and from which 4-5 ml of clear solution is given blindly at about 4 -10 sites in one sitting. By this method, reported from India,28% reported complete relief at 6 weeks 57% after second injection and 11% after 3 rd injection.

Surgical procedures

1. Division of dorsal root/tracotomy.
2. Rhizotomy (Surgical separation of pain fibers)
3. Electro coagulation of well defined area of dorsal root.
4. Electrical stimulation of thalamus and spinal cord
5. Anterolateral cordotomy.

Prevention of herpes zoster

Zoster vaccine live (Oka/Merck)

A subcutaneously administered live high titer (18,700 to 60,000 plaque forming units per dose) Varicella zoster virus vaccine of oka/Merck strain has been evaluated for prevention of herpes zoster and reduction of zoster associated pain in adults aged 60 years or above.

AIM OF THE STUDY

A. **The Study of clinical spectrum of Herpes zoster was undertaken to find out**

1. Age Distribution
2. Sex Distribution
3. Prevalence of Prodromal symptoms
4. Prevalence of presenting complaints and

   Constitutional symptoms
5. Pattern of dermatomal involvement
6. Prevalence of Risk factors
7. Association with cutaneous and systemic diseases if any.
8. Prevalence of complications

B. Therapeutic Trial

To compare the efficacy of Famcyclovir 500 mg 3 times daily Vs Acyclovir 800 mg 5 times daily for 7 days of 10 cases each.

MATERIALS & METHODS

A. Clinical Study

The study was conducted between August 2007 and July 2009 at the department of dermatology, Chengalpattu Medical College, Chengalpattu, on 30 cases of herpes zoster. All cases of herpes zoster attending skin out patient department and referred cases of zoster from other department were studied.

Preliminary information including demographic data was taken from all patients followed by a clinical examination. This included general physical examination, complete systemic examination and thorough dermatological examination. A detailed history regarding the prodromal and presenting symptoms, day of occurrence of skin lesions, nature of pain and its intensity and duration, and other symptoms if any, were elicited and recorded. Also, history of chicken pox and previous attack of herpes zoster was noted. History suggestive of provocative factors like drug, recent trauma, surgical manipulation of spine, irradiation, immunosuppression, and tumor involvement of cord and ganglion are noted.

Patients were screened for signs and symptoms of cutaneous, systemic and neoplastic diseases and also diabetes mellitus, pulmonary tuberculosis and exposure to the risk of sexually transmitted diseases,

A thorough dermatological examination regarding the following features like segment (s) involvement, morphological pattern of lesions, presence of tenderness/hyperesthesia, lymphnode enlargement, dissemination of lesion in other areas of the body and other dermatological diseases related or unrelated to zoster.

Whenever necessary, opinions from ophthalmologist, neurologist, chest physician and general physician were sought.

Diagnosis of herpes zoster lesion was made clinically. Investigations such as Tzanck Smear (in Leishman's Stain), skin biopsy, complete hemogram, urine examination, blood sugar, blood VDRL, ELISA and radiological examinations were carried out in relevant patients.

All Patients were treated with acyclovir 800 mg 5 times daily For 7-10 days .Antibiotics, analgesics were also instituted in some of cases, with topical application included calamine lotion,
1% silver sulfadiazine.

All the patients were treated in the outpatient department and subsequently they were followed depending upon the cases and complications encountered, till the resolution of signs and symptoms. Complications like secondary bacterial infection, ulceration, delayed

healing, scarring, and post herpetic neuralgia were also noted and treated accordingly.

A. Therapeutic trial

This randomized prospective comparative study was carried out at chengalpattu Medical College, Chengalpattu, during the year from August 2008 to August 2009 on 20 herpes zoster patients. The patients were assigned into two groups.

Group I

Includes 10 patients in whom Acyclovir 800 mg 5 times a day was given for 7 days

Group II

Includes 10 patients in which Famcyclovir 500 mg 3 times a day was given for 7 days

Inclusion criteria

The following patients were included in the study

1. Age over 18 years

2. Patients presenting within 72 hrs of onset of lesions.

Exclusion criteria

1. Patients with visceral involvement.

2. Patients with motor neuropathies, encephalitis or cerebro vascular

complication.

3. Pregnancy or lactating females.
4. Patients with concurrent malignancies.
5. Patients with auto immune diseases.

Efficacy assessment

Patients were evaluated for pain and healing of cutaneous lesion on each of 7 days which receiving treatment and every other day for 7 days post therapy then every 7 days for at least a total of 4 months

A.CLINICAL SPECTRUM

1. AGE SEXWISE PREVALENCE OF ZOSTER

Table -1

S.No.	Age group	Male	Female	Total no. of cases	Percentage (%)
1	1- 10	0	1	1	3.3
2	11- 20	1	0	1	3.3
3	21-30	1	3	4	13.3
4	31-40	2	1	3	10.0
5	41- 50	3	2	5	16.7
6	51- 60	5	3	8	26.7
7	61- 70	3	3	6	20.0
8	71- 80	1	0	1	3.3
9	81- 90	1	0	1	3.3
	Total	17	13	30	

Out of 30 cases, 17 cases were males and 13 were females.

Age wise distribution (Table-1) Shows that 14 cases were below the age of 50 and 16 were above the age of 50 years.

Maximum numbers of cases were seen between the age group of 51 to 60 years (26.7 %) and 61 to 70 years (20%) this was followed by 41 to 50 years (16.7 %) and 21 to 30 years (13.3 %). Minimum number of cases were observed in the age group of 1 to 10 years (3.3%), 71 to 80 years (3.3%). and 81 to 90 years (3.3%).

The youngest was 9 years and oldest was 81 years of age, Out of 30 cases, 17

were males and 13were females and the sex ratio is 1.30:1(male: female) approximately.

2. PREVALENCE OF PRODROMAL SYMPTOMS

The following prodromal symptoms were recorded.

1. Pain

2. Burning sensation.

3, Constitutional symptoms (Fever, Headache)

Prodromal symptoms were present in 23 cases and absent in 7 cases. Pain prior to the onset of skin rash was the commonest prodromal symptom in 50%.The next common prodromal symptom seen was burning sensation in 13.3%. Constitutional symptoms (Fever, Headache) were present in 13.3%.

PREVALENCE OF PRODROMAL SYMPTOMS

Table -2

S.No.	Prodromal symptoms	Total no. of cases	Percentage (%)
1	Pain	15	50.00
2	Burning sensation	4	13.33
3	Constitutional symptoms	4	13.33
4	Absence of Prodromal symptoms	7	23.33

3. PREVALENCE OF PRESENTING COMPLIANTS AND CONSTITUTIONAL SYMPTOMS

Main presenting complaint was skin rash. The other presenting complaint was pain. In 50 % of cases pain was present prior to the onset of skin rash and the remaining 33.3% of cases developed pain during evolution of skin rash.

The constitutional symptoms presented were fever, headache, myalgia and joint pain.

4. MORPHOLOGY OF LESION AND PATTERN OF DERMATOME INVOLVEMENT

The most common dermatome affected was thoracic dermatome(40%) followed by an area of ophthalmic branch of trigeminal nerve in 10% of cases, cervical in 10% of the cases and lumbar segment in 7% of the cases.

Thoracolumbar and cervicothroraic involvement was 6.67% and3.3% respectively. The least common dermatome involved was sacral dermatome (3.3%).

The pattern of dermatome involvement was almost similar in both sexes. 97% of patient presented with grouped vesicles on an erythematous background in dermatomal distribution. The remaining 3% of cases presented with erosions, crusting and pustules.

PATTERN OF DERMATOME INVOLVEMENT

Table - 3

S.No.	Dermatome	Sex		Side		No. of cases	Percentage (%)
		Male	Female	Left	Right		
1	Thoracic	10	2	6	6	12	40.00
2	Lumbar	1	1	1	1	2	6.67
3	Cervical	2	1	1	2	3	10.00
4	Sacral	0	1	1	0	1	3.33
5	Thoraco Lumbar	2	0	1	1	2	6.67
6	Cervico thoracic	1	0	0	1	1	3.33
7	Opthalmic	2	1	2	1	3	10.00
8	Maxillary	1	1	1	1	2	6.67
9	Mandibular	1	1	2	0	2	6.67
10	Herpes zoster oticus	1	1	2	0	2	6.67
	Total	21	9	17	13	30	

5. MULTIDERMATOMAL INVOLVEMENT AND DISSEMINATION

Multidermatomal involvement was noted in a female case (45 years) of herpes zoster with HIV positive. She had involvement of cervical dermatome C2 to C5 segments.

No recurrence of Herpes zoster was observed in any case.

6. LYMPH NODE ENLARGEMENT

Regional lymph node enlargement was noted in 95% of cases. Nodes were tender in 80% of cases and non tender in 15 % of cases and are firm in consistency.

7. PREVALENCE OF RISK FACTORS

Out of 30 cases, 8 cases were having one or more suspected risk factors. Among the 8 cases 2 were having HIV(25%), 3 were having diabetes (50%)and 3 were on steroid therapy for various other problems(25%).

PREVALENCE OF RISK FACTORS

Table -4

S.No.	Provocative Factors	Male	Female	Total no. of cases	Percentage (%)
1	HIV	1	1	2	25
2	Diabetes	3	1	4	50
3	Steroid therapy	1	1	2	25
	Total	5	3	8	

8. PAST HISTORY OF CHICKEN POX

Out of 30 cases, 90 % gave definite history of of chicken pox. 10 % of patient did not give any history of chicken pox. Of these 90%of patients, 33 % of cases gave history of chicken pox between 11 to 20 years of age and 30% of cases gave history of varicella between 1 to 10 years of age.

AGE GROUP WISE PAST HISTORY OF CHICKEN POX

Table -5

S.No.	Age group	Male	Female	Total	Percentage (%)
1	1-10 Years of age	6	3	9	30.0
2	11-20 Years of age	6	4	10	33.0
3	H/O Chicken pox in childhood (exact age is not Known)	5	3	8	27.0
4	No History of chicken pox	2	1	3	10.0
	Total	19	11	30	

9. ASSOCIATED CUTANEOUS AND SYSTEMIC DISEASES

Cutaneous diseases seen in association with herpes zoster were acne 1 case. Seborrhoeic dermatitis two cases, tinea vesicular 2 cases, Hansen's disease 1 case, insect bite allergy 2 cases ,wart 1 caser ,cellulites 1 case ,oral candidiasis 1 case ,tinea cruris 1 case and intertrigo 1 case.

The associated systemic diseases were hypertension (2 cases), bronchial asthma (2 cases) and tuberculosis (I case).

10. INVESTIGATIONS

Complete hemogram was within normal limits except for increased ESR in 2 patients, increased neutrophil count in 1 patient, and decreased hemoglobin value in 4 patients.

Blood sugar was elevated above the normal value in 7 patients. Urine routine examination was normal in almost all patients (98%).Urine examination showed reducing sugar in 2 patients with elevated blood glucose value.

ELISA test for HIV was done in all patients .Positive ELISA test result was obtained in 2 patients .One patient already diagnosed as HIV positive and presented with zoster during the course of HIV disease.

ECG was taken for patients with zoster involving left thoracic segment and it was found to be normal. Diabetologist opinion for 4 patients, neurologist opinion for 1patient, ophthalmologist opinion for 2 patients.

Tzanck smear showed multinucleated giant cells and ballooned epithelial cells in 95% of cases. Skin biopsy was done in willing patients which under light microscope in eosin and haematoxylin(H&E) staining showed intraepidermal uniloculated to multiloculated bullae with ballooned epithelial cells and multinucleated giant cells. Reticular degeneration seen in some areas. The upper dermis showed inflammatory infiltrate composed of lymphocytes, monocytes and few eosinophils.

11. COMPLICATIONS

a. Secondary bacterial infection

Secondary bacterial infection was reported in 4 cases (36.36%). In 2% of patients affected with secondary infection scarring occurred in affected dermatome. Cases were treated with topical Silver sulphadiazine cream and systemic antibiotics in addition to acyclovir.

b. Scarring

Scarring was noted in 2 cases (18.8%), which were associated with secondary bacterial infections and later developed ulceration.

C. Post herpetic neuralgia

PHN is the most feared complication in immunocompetent patients. Both the incidence and duration of post herpetic neuralgia are directly correlated with the patient's age. Out of 11 patients with complications of zoster,5 cases (45.5%) developed post herpetic neuralgia.

Among the 5 cases of post herpetic neuralgia,3 were males and 2 were females.

PREVALENCE OF COMPLICATIONS

Table-6

S.No.	Complications	Male	Female	Total	Percentage (%)
1	Scarring	2	0	2	18.18
2	Secondary bacterial infection	3	1	4	36.36
3	Post herpetic neuralgia	3	2	5	45.45
	TOTAL	8	3	11	

B.THERUPETIC TRIAL

1. TIME TAKEN FOR RESOLUTION OF LESIONS

Table-1

Patients S.No.	DRUG	
	ACYCLOVIR	FAMCYCLOVIR
	Duration in days	Duration in days
1	12	11
2	14	12
3	-	11
4	14	14
5	12	-
6	22	12
7	11	15
8	14	17
9	18	13
10	-	10

Medium time for resolution of lesion was 14.6 days in acyclovir group and 12.8 days in famcyclovir group. The difference in time taken for resolution of lesions between acyclovir and famcyclovir was not significant (P=0.78)

2. INCIDENCE OF POSTHERPETIC NEURALGIA

Table-2

Patients S.No.	POSTHERPETIC NEURALGIA	
	ACYCLOVIR	FAMCYCLOVIR
1	Present	Absent
2	Absent	Absent
3	Absent	Absent
4	Absent	Present
5	Absent	Absent
6	Present	Absent
7	Absent	Absent
8	Absent	Absent
9	Present	Absent
10	Absent	Absent

Post herpetic neuralgia was present in 30 % of the cases with Acyclovir group and 10% of the cases with famcyclovir.

DISCUSSION

A. Clinical Spectrum

Herpes zoster is common among immunocompromised persons, so the elderly are at particular risk because immunocompetence declines with age. Whitley et al[51] reported that zoster affects 20% of general population during their life time, especially in elderly. This study of 30 patients with herpes zoster revealed that the majority of the patients affected were adults in the fifties (26.7), and sixties (20 %).This is in accordance to the observation made earlier in other studies [25] where in most cases are in the age group above 50 years with highest incidence among individuals in the sixth to eighth decades of life.

Total number of cases in childhood and adolescence age group were 3 in number.

In this study male: female ratio was 1.3:1 which is in accordance to the western studies [52] ,where both males and females were equally affected.

Prodromal symptoms were in 23 cases (76%) in this study .In majority of cases, pain was the commonest prodromal symptom.

In this study, majority of the cases (74%) presented between 2 to 5 days and the remaining 26% of cases presented between 6 to 8 days and above, which is similar to the study report given in western literature[25.]

Most common presenting symptom in this study was pain and skin rash was the next common presenting complaint which is similar to various study reports[25,]

53

Constitutional symptoms were noted in 75% of cases in this study.

In this study, 97% of cases had classical herpes zoster in dermatomal pattern[25] and 3% of cases had crusting and erosions.

Thoracic dermatome was the most common dermatome involved (40%) in this study, followed by cervical and ophthalmic dermatome in 10% of cases each and lumbar dermatome in 6.7% of cases, in accordance with the literature reports [33]. The least common dermatome involved was sacral segment.

Out of 30 cases, 97% of cases had localized involvement with grouped vesicles and 1% of cases had multi dermatomal involvement. Multidermatomal zoster was seen in a case with underlying immunodeficiency (HIV infection).

Eight cases were having one or more suspected risk factors. Out of 8 cases, most common risk factors seen was diabetes in 4 cases (50%),HIV infection in 2 cases (25%) and 2 cases (25%) on steroid therapy.

Past history of chicken pox was given by 90% of cases. The remaining 10% of cases were either not aware of or not had chicken pox.

Systemic disease seen in association with herpes zoster was hypertension 2 cases, bronchial asthma 2cases, and tuberculosis 1case.

Few cutaneous disease seen in herpes zoster patients in this study were acne, tineaversicolor, seborrheicdermatitis insectbiteallergy, Hansen's disease, cellulitis, oralcandidiosis, tineacruris and intertrigo, one case each.

Tzanck smear was positive in 95% of cases and it was negative in 5% of cases and this correlates well with that of literature reports[25] .Complete hemogram was normal in 80% of cases in this study. This is in contrast to the literature reports, where in normal complete hemogram are reported in zoster patients.Raised ESR was noted in 2 patients and decreased hemoglobin value was noted in 4 patients.

Blood sugar was elevated in above normal value in 4 patients.Urine routine examination was normal in almost all patients (98%).Urine examination showed reducing sugar in 2 patients (6.6%).

In this study, 2 cases out of the 30 patients who were tested for HIV were sero positive. Among the 2 cases of HIV positivity, herpes zoster was the presenting disease for HIV infection in 1 case. Recurrence of zoster in HIV positive patients were not observed in this study.

Skin biopsy showed histopathological features as described in literature [25/11].

ECG was taken for all cases with lesions involving left upper thoracic dermatomes and no abnormality was detected.

Post herpetic neuralgia was the commonest complications noted in 5 patients (45.45%) followed by secondarybacterialinfection in 4cases (36.36%), scarring in 2 cases (18.8%) .

In accordance to the literature reports, the incidence of post herpetic neuralgia increased with increasing age in this study.

Therapeutic trial

- In Total, 20 patients were enrolled in the study and divided into two groups.
- In Group I: 10 patients were given Tab Acyclovir 800 mg 5 times/day for 7 days.
- In Group II: 10 patients were given Tab Famcyclovir500mg 3 times/day for 7 days.
- Out of 10 patients in Group I: 2 patients did not complete the study. The reason was due to
  (i) Deviation from protocol.
  (ii) Loss of follow up.
- Out of 10 patients in group II: 1 patient did not complete the study. The reason was due to loss of follow up.
- In this study, median time for resolution of lesions was 14.6 days in group I and 12.8 days in Group II, this is inaccordance with literature report[55.]
- During treatment, 5 patients in group I had adverse effects such as constipation, dysuria, headache, nausea and 2 patients in group II had side effects such as head ache and nausea. The frequency of adverse effects was low in group II compared to group I.
- The incidence of PHN in group I was 30%.and group II was 10%, this is inaccordance with literature report[55.]

Conclusion

- In this study, herpes zoster mainly occurred in fifth and sixth decades of life.
- No sex preponderance in incidence was found with the sex ratio of 1.3:1
- Prodromal symptoms were present in 76 % of cases and pain was the commonest prodromal symptom.
- Most common presenting symptom was pain followed by skin rash.
- Thoracic dermatome was the most common dermatome involved and sacral segment was the least common dermatome affected.
- The risk factors noted were diabetes, HIV infection and steroid therapy.
- HIV infection was present in 2 cases. Out of 2 cases, 1 case was already diagnosed as HIV positive and developed herpes zoster during the course of HIV disease. This indicates the importance of HIV testing in all patients presenting with herpes zoster, especially in patients below age of 50 years.
- The systemic diseases associated with herpes zoster were

hypertension, bronchial asthma and tuberculosis.

- No significant association of herpes zoster was found with any other skin disorder in this study.
- Duration of time taken for resolution of lesions, ranged from 2 to 3 weeks.
- Post herpetic neuralgia was noted in patients with increasing age.

Therapeutic Trial

This study indicates that Famcyclovir is more effective than Acyclovir interms of parameters such as incidence and duration of post herpetic neuralgia, patient's compliance and adverse effects. However, there was no statistical significant difference in the duration of resolution of lesions between acyclovir and famcyclovir treated patients (P=0.78)

BIBLIOGRAPHY

1. Von Bokay J.Uber den aetiologischen Zusammenhang dervarizellen mit geswissen fallen von herpes zoster wien Wochenschr,22:1323,1909.

2. Steiner P.Zur Inokulation der vaicellu.Wein Med Wochenschr.1875:25:306.

3. Kundratitz K.Experimantal ubertragwagen von herpes zoster auf menschen und die beziehungen von herpes zoster varicellu.Z Kinderheilkd 1925:39:379.

4. Garland J.Varicella following exposure to herpes zoster.N Engl J Med.1943:228:336.

5. Seiler HE.A study of herpes zoster particularly in its relationship to chickenpox.J Hyg.1949:47:253-262.

6. Tyzzer EE. The histology of skin lesions in Varicella and herpes zoster:serologic studies with the viruses as propagated in vitro.J Exp Med.1958:228:336-337.

7. Lipschutz B.Untersuchungen uber die Atloogies der krankheites der Herpes Gruppe(Herpes Zoster,Herpes geniitalis,Herpes febrilis)Arch dermatol Syph.1921:136:428.

8. Weller Th,Witton HM.The etiiologic agent of varicella and herpes zoster:Serologic studies with the viruses as propagated in vitro.J Exp Med.1958:336-337.

9. Hope-Simpson RE: The nature of herpes zoster: along term study and a new hypothesis. Proc R Soc Med 58:9, 1965.

10. Arvin AM,Pollard RB, Rasmussen L.Merigan T:Selective impairment in lymphocyte reactivity to Varicella-Zoster antigen among untreated lymphoma patients J Infect Dis,137:531,1978.

11. Grossman MKC and Silvers DN. The Tzanck Smear: Can Dermatolologists accurately interpret it? Journal of American academy

of Dermatology, 27:403-5, September 1992.

12. Roxas M (2006).Herpes Zoster and PHN. Diagnostic &therapeutic considerations. Alternative medichine Review.A Journal of clinical therapeutic 11(2):102-13.

13. J Am Acad Dermatol 1988 Jan:18:176-9.

14. Rev Med Interne 2007 March 28(3):166-72.

15. Almeida JD.Howatson AF.Williams MG. Morphology of Varicella (Chickenpox)virus.virology,1962:16:353.

16. Davision AJ Varicella-Zoster Virus.The Fourteenth Fleming Lectures.J Gen virol,72:475,1991.

17. Gershon A,ZhuZ,Sherman DL et al:Intracellular transport of newly synthesized VZV:final envelopment in the trans-golgo network,JVirol,68:L6372,1994.

18. Werller TH,serial propagation in vitro of agents producing inclusion bodies derived from Varicella and herpes zoster.Proc Soc Exp

19. Biol Med,1953:83:340-346.

20. Guss HA,Broughoton DD.Melton LJ et al Epidemiology of Herpes Zoster in children and adolescents,a population based study.Paediatrics 76:512,1985.

21. Nagasako EM,Johnson RW,Griffin DR,et al:Gerographic and Racial aspects of herpes zoster.J Med Virol.2003:70 Suppl 1:S20-3

22. Peto TEA and Jwel-jenson BE.Varicella Zoster virus infection ,In: Oxford text book of medichine,3 rd edition.weatherall DJ,Leadingham JGG and warell DA.Eds,Oxford:Oxford university press,1996.Vol I:346-351.

23. Liedtke W.Opelka B,Zimmerman Ca,Liquit E .Age distribution of latent herpes simplex virus-I and vericella Zoster virus genome in Human nervous tissue.J.Neurol SCi 1993:116:6-11.

24. Clarke P.Beer T.Cohrs R.Configiguration of latent VZV DNA.J Virol 1995:69:8151-8154.

25. Oxman MN and Rhoda Alani.Vericella and herpes Zoster.In:Dermatology in general medichine, 4th Edition.Thomas BFitspatrick et al.Eds.Newyork:MC Graw-Hill Incl.,1993.Vol.2:2543-2572.

26. Huff JC,Krueger GG,Overall Jc Jr et al.The Histo-Pathologic evaluation of recurrent herpes simplex labialis.J Am Acad Dermatol 1981:5:550-557.

27. Neal Penney's diseases caused by viruses In: lever's Histopathobhy of the skin, Eighth edition. David Elder et al,Eds.Philadelphia:Lippincott-Raven publishers,1997.p 569-589.

28. Erhard H.Runner Tm,Kreinkamp M et al Atypical Varicella zoster virus infection in an immuno compromised patients :"result of a virus induced vasculititis.J Am Acad Dermatol 1995:32:908-911.

29. Nikkels AF.Snoeck R,Renitier B ,Piered GE,Chronic verucous vermicelli zoster virus skin lesions, Clinical ,histological,molecular and therapeutic aspects.clin Exp.Dermatol 1999:24:346-358.

30. Steinberg S.Gershon a antibodies to Varicella zoster virus by using latex agglutination test.J.Clin Microbiol,29:1527,199.

31. Uduman SA,Gershon AA, Brunell PA.Should patients with zoster receive zoster immune globulin.JAMA,234:1047:1975.

32. Arvin A,Korop chak C.Sharp M et al:The T-lymphocytes response to Varicella-Zoster viral proteins.P-71.Advances in experimental medichine and Biology.Vol.278.Plenum.New York.1990.

33. J.C.Sterling, viral Infection in Rook's Text book of dermatology, Vol II, 7 th editition,2004.page 25.22 to 25-29.

34. 34.Seghal VN,Kumar S.Jain s.Typical Varicella zoster opthalmicus 2000:14:59-60.

35. Rifkind D.The activation of Varicella Zoster viral infections by immumosuppressive therapy.J Lab clin Med 1966:68:463-74.

36. Thomas P.Habif ,Herpes zoster: In Clinical Dermatology Fourth edition.Edited by :Mosby ,St.Louis,USA.Page -394 to 408.

37. Tomkinson A.Roblin DG,Brown MJ.Hutchinsion's Sign and its importance in Rhino logy,Rhino logy 1995:33(3):180-182.

38. Umesh RE.Herpes Zoster opthalmicus and HIV infection in Nigeria,Int J STD AIDS 1998:9:476-479.

39. Juel Jenson BE.Mac callum Fo.Herpes Simplex,Varicella and zoster London:Heinemann,1972.

40. 40.Palexas GN.Welsh NH,Herpes Zoster Opthalmicus an early point to HIV -1 Positively in young African Patients .Scand J Immunol Supple 1992,11:67-68.

41. Nally FF,Ross IH.Herpes Zoster of oral and facial structures. Reports of 5 cases and discussion.Oral surg.oral med.Oral pathol. 32:21-34.

42. Robillard RB,Hil Singer RL.Adout K.Ramsay-Hunt facial paralysis: clinical analysis of 185 patients.Otolarynglology,Head and neck Surgery 1986:95:292-297.

43. Scott Mj Sr.Scott Mj Jr,Ipsilatyeral deafness and herpes zoster opthalmicus.Arch dermato 1983:119:235.

44. Mc Govern and Fitz Hugh-Arch Otolarynglogy 55:307,1952.

45. Yamanishi T.et al Urinary retention due to herpes virus infections.Neuro Uro; Urodyn 1998: 17:613.

46. Hailey –Southern Med J1:47:728,1954.

47. Walls –Brit.Med 1:496,1942.

48. Salvin et al –Amer .J med 8: 456.1950(Recurrent herpes simplex in zoster distribution)

49. Heskell NS,Hanifin Jm,"Recurrent herpes zoster" An unproved entity J

Ame acad Dermato; 1984,:10,486-490.

50. Dover JS.et al .Cutaneous manifestations of HIV infection part -1 Arch,Dermatol.1991:1237:1388-1391.

51. Whiteley RJ.Varicella zoster virus.In:Principles and practice of infections diseases 4 th Edition. Mandell GL.Bennet JE and Raphael Dolin,Eds.New York:Churchill Livingstone,USA,1995.Vol2:1345-1351.

52. Liesegang TJ and Rochester MN.The Varicella zoster virusSystemic and ocular feautures.Journal of American Academy of dermatology,11:165-191,1984.

53. Highet AS & Kurtz J.Viral infections In:Textbook of Dermatology,5th Edition,Chapion RH,Burton JL and Ebling FJG,Eds Oxford: Blackwell scientific publi9cations,199.Vol 2:867-952.

54. Herpes zoster and postherpetic neuralgia incidence and risk indicators using a general practice research database :Wim opstelten, Jan W Mauritz.

55. Double –blind randomized acyclovir-controlled parallel gp trial comp-airing the safety &efficacy of famcyclovir & acyclovir in patients with uncomplicated Herpes zoster:Meng-chuon(Taiwan Study)

56. Therapy with Acyclovir and Valaciclovir on Prolonged Pain

M. J. Wood, S. Shukla, A. P. Fiddian,* and R. J. Crooks Department of

Infection, Heartlands Hospital, Birmingham, and Glaxo

57. Wood MJ. Herpes zoster and pain. Scand J Infect Dis 1991; 78(suppl): 220.53–61. 15. So¨ltz-Szo¨ts J, Tyring S, Andersen PL, et al. A randomized controlled

58. Degreef H, Famciclovir Herpes Zoster Clinical Study Group.

Famciclovir, a new oral antiherpes drug: results of the .rst controlled clinical studydemonstrating its efficacy and safety in the treatment of uncomplicatedherpes zoster in immunocompetent patients. Int J Antimicrob Agents 4:241–246 (1994).

59. Tyring S, Barbarash RA, Nahlik JE, et al. Famciclovir for the treatment of acute herpes zoster: effects on acute disease and postherpetic neuralgia. Randomized, double-blind, placebo-controlled trial. Collaborative FamciclovirHerpes Zoster Study Group. Ann Intern Med 123(2):89–96 (1995 Jul).

60. Dworkin RH, Boon RJ, Griffin DR, Phung, D. Postherpetic neuralgia:impact of famciclovir, age, rash severity, and acute pain in herpes zosterpatients. J Infect Dis 178(Suppl 1):S76–80 (1998 Nov).

PROFORMA

S.No: **OP/IP No:**

Name: *Age* *Sex*

Occupation: **Address:**

PRESENTING COMPLAINTS:

H/O PRESENTING ILLNESS

1. H/o. Pain Onset- Prehepetic/Herpetic

   Nature-Burning/Tingling/Deep boring/Lancinating
2. H/o cutaneous lesions: Papules/Vesicles/Grouped /Diffuse
3. H/o Paraesthesia
4. H/oConstitutional Symptoms: Fever, Malaise, Headache.
5. H/o Itching, tingling, numbness over the involved site.
6. H/o Difficulty in swallowing.
7. H/o Pain &Photophobia in eye.
8. H/o Watering in eye.
9. H/o Toothache (Oral facial Zoster)
10. H/o Otalgia
11. H/o Difficulty in urination /defaecation
12. H/o Precipitating Factors/predisposing Factors- Stress, Trauma, Radiation,

    Recent surgery, organ transplantation,

    Systemic conditions: DM/Malignancy

PAST HISTORY

H/o Varicella

H/o Contact with Chickenpox/Herpes Zoster.

H/o Diabetes/ TB/ HT

H/o Recurrent Zoster

TREATMENT HISTORY

H/o Treatment for Malignancy

H/o Steroid Therapy /other immunosuppressive drug therapy

H/o Treatment for HIV

H/o Treatment for Diabetes.

H/o Radiotherapy

FAMILY HISTORY

H/o Varicella in any other family members (for contact exacerbation).

PERSONAL HISTORY

H/o Alcoholism/Smoking

MENTURAL HISTORY

SEXUAL HISTORY

Hetero/homo/Bisexual Protected/unprotected

Known/unknown partner

Single/Multiple partner

GENERAL EXAMINATION

Built&Nourishment

Pallor, Icterus, Edema, Lymphadenopathy (Regional/Generalized)

Eyes,

Vitals: Febrile/Afebrile.

SYSTEMIC EXAMINATION

CVS: RS:

ABD: CNS:

DERMATOLOGICAL EXAMINATION

1. Site of the lesion - Dermatome involved
2. Morphology - Erythema/ Papules/ vesicles/ Crust/ Erosion
3. Pattern - Grouped / Localised/Dissminated/Multidermatome
3. Sensory involvement- Tenderness/Hyperesthesia
4. Motor involvement - Cranial nerves/Trunks/Limbs

5. Mucous Membrane - Eyes/Oral Mucosa/Genital Mucosa
6. Nails and Hairs
7. Palms and Soles
8. Complications:

Cutaneous - Secondary infection/ulceration
Scarring- Atrophic/Hypertrophic/Keloidal Anesthetic/
Pigmented /Depigmented
Phantom hernia

Eye complication

Neurological complication: Post herpetic neuralgia/others

Visceral complication: Respiratory Tract/**GIT/GUT**

INVESTIGATIONS

1. Blood TC, DC, and ESR, Hb%
2. Urine albumin, Sugar, Deposit
3. Blood Sugar, Urea
4. Serum creatinine
5. Tzanksmear
6. Blood VDRL
7. ELISA
8. Skin Biopsy (If necessary)
9. ECG (If necessary)
10. CXR PA view
11. USG abd(Selected Case)

TREATMENT

Symptomatic Treatment

Antiviral Treatment

A. T.Acyclovir 800 mg 5 times a day for 1 week

B.T.Famcyclovir 500 mg 3 times a day for 1week

Follow up; (for 4 months)

Variables	Acyclovir	Famcyclovir

- Time taken for resolution of lesions
- Incidence of post herpetic neuralgia.
- Adverse effects

Acronyms

l.No	Acronyms	Expansion
1	PHN	Post Herpetic Neuralgia
2	HIV	Human Immuno Deficiency Virus Infection
3	FCV	Famcyclovir
4	ACV	Acyclovir
5	Carbamaz	Carbamazepine
6	ESR	Erythrocyte sedimentation Rate
7	ELISA	Enzyme Linked Immuno Sorbent Assay
8	RFT	Renal Function Test
9	ECG	Electro Cardiogram
10	CRF	Chronic Renal Failure
11	HT	Hypertension
12	Hb	Hemoglobin
13	IBA	Insect Bite Allergy
14	TB	Tuberculosis
15	Rt	Right
16	Lt	Left
17	TV	Tinea versicolor
18	VZV	Varicella Zoster Virus